

REMARKS

Claims 1-29 constitute the pending claims in the present application, and claims 1, 2, 5, 6, 9, 10, and 13-25 are currently under consideration. Applicants cancel, without prejudice, previously withdrawn claims 3-4, 7-8, 11-12, and 26-27. Applicants reserve the right to prosecute claims of similar or differing scope in a continuation or divisional application.

Applicants add new claims 30-36. Support for the subject matter of these claims is found throughout the specification. Specific support can be found, for example, on page 34, line 21- page 37, line 6. No new matter has been entered.

The enclosed preliminary amendment accompanies Applicants' Request for Continued Examination (RCE). Applicants respectfully request reconsideration in view of the following remarks. To expedite allowance of the pending claims, Applicants briefly address the Issues raised by the Examiner in the previous Office Action.

1. Applicants note with appreciation that the amendments put forth on December 9, 2004 have been entered in full.
2. Applicants note with appreciation that any objections or rejections that were not expressly maintained in this Office Action have been withdrawn.
3. Claims 1, 2, 5, 6, 9, 10, and 13-25 are rejected under 35 U.S.C. 103(a) as allegedly unpatentable over the US Patent No. 6,639,051 (the "051 patent") in view of Ericson et al. and US Patent No. 4,816,567 (the "567 patent"). Applicants traverse this rejection and contend that the rejection is moot in light of the amended claims.

To establish a *prima facie* case of obviousness, one of skill in the art must have been motivated to combine the cited references to arrive at an invention that meets each and every limitation of the pending claims. Specifically, as indicated in MPEP 2143.01, "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." Furthermore, obviousness requires that one of skill in the art had a reasonable expectation of success at arriving at the claimed invention by combining or modifying the cited references. MPEP 2143.02. Neither of

these requirements have been satisfied, and thus the cited references fail to render the claimed invention obvious.

To briefly reiterate, Wang et al. fail to specifically teach the use of anti-hedgehog antibodies as hedgehog antagonists. While Ericson et al. teach the use of anti-hedgehog antibodies, Ericson et al. teach the use of such anti-hedgehog antibodies in an entirely different in vitro neuronal tissue explant system (e.g., floor plate explants). The teachings of Ericson et al. provide no motivation to extend the results gathered in a particular in vitro neuronal explant system to non-neuronal systems such as hair. Absent motivation to combine the references, the combination of Wang et al. and Ericson et al. fail to satisfy the criteria necessary for rendering the claimed invention obvious. Furthermore, the scant evidence offered by Ericson and obtained in a completely different explant system fails to provide one of skill in the art a reasonable expectation of success for combining the teachings of Ericson et al. and Wang et al. to arrive at Applicants' invention.

Additionally, Applicants point out that the presently claimed methods encompass several distinct physiological effects caused by administration of anti-hedgehog antibodies: inhibition of growth or differentiation of epithelial cells; inhibition of proliferation of epithelial cells; inhibition of hair growth; and inhibition of proliferation of hair follicle cells. Neither Wang et al. nor the combination of Wang et al. and Ericson et al. teach or suggest that anti-hedgehog antibodies could have these effects on non-neuronal cells and tissues; as required by the pending claims.

The Examiner additionally cited US Patent No. 4,816,567 (the "'567 patent") which, in combination with Wang et al. and Ericson et al., allegedly renders the claimed invention obvious. As outlined in detail above, to render an invention obvious, there must be some motivation to combine the cited references. Such motivation does not exist here. The '567 patent provides general teachings directed to making chimeric antibodies. The '567 patent does not teach or suggest anti-hedgehog antibodies, or that anti-hedgehog antibodies can be used to antagonize hedgehog signaling. Furthermore, the '567 patent does not teach or suggest that hedgehog antagonists generally, or anti-hedgehog antibodies specifically, can be used to modulate any of the following physiological activities: inhibition of the growth or differentiation of epithelial

cells; inhibition of the proliferation of epithelial cells; inhibition of hair growth; and inhibition of the proliferation of hair follicle cells. Given that the general teachings of the '567 patent are entirely unrelated to the subject matter of the present application, one of skill in the art would have no motivation to combine this reference with either Wang et al. or Ericson et al.

Furthermore, even if one of skill in the art would have been motivated to combine the '567 patent with Wang et al. and Ericson et al., the '567 patent fails to overcome the deficiencies of Wang et al. and Ericson et al. Specifically, and as outlined in detail above, one of skill in the art would not have had a reasonable expectation of success of combining Wang et al. and Ericson et al. to arrive at the claimed invention. The '567 patent provides only general teachings in the making of chimeric antibodies, and does not increase the likelihood of successfully identifying and using anti-hedgehog antibodies to inhibit the growth and/or proliferation of non-neuronal tissues include epithelial tissue and hair.

Applicants maintain that the cited references fail to establish a prima facie case of obviousness. Nevertheless, to expedite prosecution, Applicants have amended the claims to more particularly point out certain embodiments of the claimed invention. Applicants' amendments are not in acquiescence to the rejection, and Applicants reserve the right to prosecute claims of similar or differing scope.

The amended claims are directed to the use of particular anti-hedgehog antibodies. Specifically, the amended claims are directed to the use of 5E1, AP.G6, humanized antibodies thereof, and fragments thereof. The use and benefits of these particular anti-hedgehog antibodies is taught by the present application (See, for example, page 35-36), and not by the cited references. Although Applicants maintain that one of skill in the art would not have had a reasonable expectation of success in modifying the teachings of the cited references to arrive, generically, at Applicants invention, clearly one of skill in the art would have no reasonable expectation of success at selecting *particular* anti-hedgehog antibodies for use as presently claimed. Accordingly, the cited references fail to render the claimed invention obvious.

Applicants contend that the cited references fail to teach or suggest the particular combination of elements set forth in the claims. Specifically, the cited references fail to teach or suggest methods for using *particular* anti-hedgehog antibodies (the particular composition

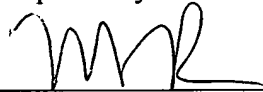
recited in the pending claims) to inhibit cells of *particular* tissues, for example hair follicle cells. These references fail to teach the benefits of the particular combination of agents and target cell types set forth in the pending claims. Furthermore, these references provide no motivation to specifically select these elements (i.e., the particular hedgehog antagonists and target cell types), as presently claimed. MPEP 2144.08 outlines the guidelines for determining that a reference renders an invention obvious and directs the Examiner to “determine whether one of ordinary skill in the relevant art would have been motivated to make the claimed invention as a whole, i.e., to select the claimed species or subgenus from the disclosed prior art genus.” Applicants contend that the cited references fail to provide motivation to select the specific hedgehog antagonists and the specific target cell types, as required by the pending claims. Reconsideration and withdrawal of this rejection is respectfully requested.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945, under order no. CIBT-P01-114.**

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Respectfully Submitted,



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